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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/687,575	10/13/00	KADDURAH-DAOUK R	AVZ-007CP3

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EXAMINER	
COVINGTON,R	
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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary	Application No. 09/687,575	Applicant(s) Kaddurah-Dauk et al
	Examiner Raymond Covington	Art Unit 1625

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Mar 5, 2001* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-63* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-63* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 3

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-63 are provisionally rejected under the judicially created doctrine of double patenting over claims 1 and 3-61 are of copending Application No. 09/285,395. This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

The subject matter claimed in the instant application is fully disclosed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application and the instant application are claiming common subject matter, as follows: a method of modulating a nervous system disorder using a creatine compound as claimed.

Furthermore, there is no apparent reason why applicant would be prevented from presenting claims corresponding to those of the instant application in the other copending application. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of specific nervous system disease (as demonstrated by the Examples 1-3 in the instant specification at pages 50-55 illustrating models for Huntington's disease, Parkinson's disease, ALS disease), comprising the administration of creatine compounds does not reasonably provide enablement for the administration of the creatine compound, wherein the administration of the creatine compounds results in

[a] **elimination** of **all symptoms** associated with a preexisting disease of the nervous system (as in claim 33); and

[b] **preventing** the occurrence of **any** or all **types** of nervous system disease within a subject (as in claim 34).

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The specification does not give any guidance as to full range of diabetic complicating disease which could be treated or prevented using the instant claimed process. In re Wands. 8 USPQ2d 1400 (1988), factors to be considered In determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. The nature of the invention,

2. The state of the prior art,

3. The predictability or lack thereof In the art,

4. The amount of direction or guidance present,

5. The presence or absence of working examples,

6. The breadth of the claims,

7. The quantity of experimentation needed, and

8. The level of the skill In the art.

In the present case [1] the breadth of the claims encompass methods for treating a subject afflicted with a nervous system disease, wherein the administration of the creatine compound reduces or **eliminates symptoms** associated with a preexisting disease disease of the nervous system (as In claim 33); or **prevents** the occurrence of a nervous system disease within a subject (as In claim 34). However, the examples In the specification teach the only the administration of creating compounds In model treatments for Huntington's disease, Parkinson's disease, ALS disease In Example 1-3 of the instant specification to yield positive or negative results; [2] the nature of the claimed invention cannot be determined In light of the foregoing and without knowing how prevention of the many different types of nervous system disease is achieved via the use of creatine compounds and corresponding analogs or derivatives; [3] and [5] the art and the level of predictability In the art is unpredictable as to: [a] the nature of preventing emergence of different nervous system disease as the specification does not teach the outright prevention of the aforementioned disease, including related symptoms, for which there is not known art-recognized

therapy. The many different types of nervous system diseases is not regarded as preventable by those skilled In the art, because there simply is no known cure. In light of the aforementioned context, use of the term "preventing" or "eliminating In the claimed invention equates to the use of the term "cure", but provides no examples of how the prevention or elimination of such diseases are effectuated; [4] and [6] the inventor provides no guidance beyond the model Examples 1-3 taught In the specification; and [7] the existence of working example are limited to aforementioned model examples as described In [6] above as taught In the instant specification.

Due to insufficient guidance, lack of working examples to support the broad breadth of claims 1-43, one skilled In the art could not predict how the methods of the claimed invention could prevent nervous system diseases.

In light of the preceding discussion, one skilled In the art **could not practice** invention **without undue experimentation**, as claims 1-43 fail to correlate reasonably with either the enabling disclosure of the specificating and the claims.

This rejection may be overcome by deleting the word "preventing" from the claims and limiting the claims to "treatment" type language. However, applicants are advised any amendments to the claims may not incorporate material not supported by the instant specification.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made In this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described In a printed publication In this or a foreign country or In public use or on sale In this country, more than one year prior to the date of application for patent In the United States.

Claims 1-24 are rejected under 35 U.S.C. 102(b) as being anticipated by Hagenfeldt et al (Muscle and Nerve, Oct. 17, 1994 (10), 1236-7).

Hagenfeldt et al. discloses the use of creatine [CAS Reg No.: 57-00-1] In a therapeutic use for the treatment of a nervous system disease In human patients, i.e., MELAS syndrome (i.e., as conventionally known In the art as a nervous system disease associated with mitochondrial myopathies and encephalomyopathies categories and defined In the art as "a mitochondrial disorder characterized by focal or generalized seizures, episodes of transient or persistent neurologic dysfunction resembling strokes, and ragged-red fibers In muscle biopsy" as defined by the National Library of Medicine: IGM Metathesaurus Information Screen).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth In this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth In section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill In the art to which said subject matter pertains. Patentability shall not be negatived by the manner In which the invention was made.

Claims 1-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hagenfeldt et al. (Muscle and Nerve, October 17, 1994, Vol. 10 pages 1236-7), Applicants admission In instant specification page 38, lines 1-18) and Schulthesis et al. (J. Of Neurochemistry, June 1990), 54 (6), 1858-63).

Hagenfeldt et al. teaches the oral dosage administration of creatine [CAS Reg No.: 57-00-1] In a therapeutic use for the treatment of a nervous system disease In human patients, i.e., MELAS syndrome (i.e., as conventionally known In the art as a nervous system disease

associated with mitochondrial myopathies and encephalomypathies categories and defined In the art as "a mitochondrial disorder characterized by focal or generalized seizures, episodes of transient or persistent neurologic dysfunction resembling strokes, and ragged-red fibers In muscle biopsy" as defined by the National Library of Medicine: IGM Metathesaurus Information Screen).

In view of the above, Hagenfeldt et al. **differ** from the claimed invention In that it **does not teach** the use of creatine In the methods of treatment nervous system disease other than MELA syndrome.

However, it is conventionally known In the art that nervous system disease include: Alzheimer's disease, Parkinson' disease, Huntington's disease, motor neuron disease diabetic and toxic neuropathies, traumatic nerve injuries, multiple sclerosis, acute disseminated encephalomyelitis, amyotrophic lateral sclerosis, acute necrotozong hemorrhagic leucoencephalitis, diseases of dysmyelination, mitochondrial diseases, fungal and bacterial infections, migrainous disorders stroke, aging, dementia and mental disorders such as depression and schizophrenia as taught by applicants own specification (see instant specification page 9, lines 13-23 to page 16, lines 1-13), Stedman's Medical Dictionary and Medline.

Schulthiess et al. teaches that studies with creatine In complex neuronal systems are of importance, because they show that creatine changes neuronal energy balance and synthesis and release of the neurotransmitter GABA. (Moreover, an admission In applicants instant specification at page 38, lines 1-18, states that "the mechanisms by which nerve cell metabolites are normally directed to specific cell tasks is poorly understood. It is though that nerve cells, like

other cells regulate the rate of energy production In response to demand. The creatine kinase system is active In many cells of the nervous system and is thought to play a role In the allocation of high energy phosphate to many diverse neurological processes...")

A person of ordinary skill In the art would have been motivated to develop methods of treating a subject afflicted with a nervous system disease other than MELAS syndrome comprising the administration of creatine, because Schulthiess et al. renders obvious that studies with creatine In complex neuronal systems are of importance, because they show that creatine changes neuronal energy balance and synthesis and release of the neurotransmitter GABA.

It would have been prima facie obvious to a person of ordinary skill In the art at the time the invention was made to modify the teachings of Hagenfedt et al. With the teachings of Schulthiess et al. to administer creatine In methods of treating different nervous system diseases that are conventionally known In the art, because creatine would be useful In the treatment of other nervous system disease as al mechanisms of action of the same compound would invariable be inherent.

Claims 44-61 are rejected under 35 U.S.C. 102(b) as being anticipated by Boehm et al (Biochimica et al. Biophysical Acta 1274 (1996) 119-128.

Boehm et al teach creative analogues as recited In the claims. See, for example, page 124 compounds of formulas (a), (c), (d) and (e).

It is noted that disclosure by a reference of species, which are within a claimed genus, is technical anticipation. In re May, 197 USPQ 601 (CCPA 1978), In re Slayter, 276 F.2d 408, 411 125 USPQ 345, 347 (CCPA 1960).

Claims 44-61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Biochimica et Biophysica Acta 1274 (1996) 119-128.

Boehm et al is applied as In the above rejection. One of ordinary skill would similar other closely structurally related compounds to have similar properties.

No claim is allowed.

Any inquiry concerning this communication should be directed to R. Covington at telephone number (703) -308-4704.

Covington/LR

September 13, 2001

Alan L. Rotman

ALAN L. ROTMAN
PRIMARY EXAMINER